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ALDEHYDE-ENAMINES FROM α-OXOCARBOXYLIC ACIDS. A FACILE AND GENERAL ROUTE TO ALDEHYDES VIA DECARBOXYLATION OF α-OXOCARBOXYLIC ACIDS CARRYING β-HYDROGENS

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SUMMARY: When α-oxocarboxylic acids carrying β-hydrogens are treated with a secondary amine in boiling benzene with azeotropic removal of water, they decarboxylate quantitatively to form aldehyde-enamines which subsequently are hydrolyzed to the corresponding aldehydes in high yields.

α-Oxocarboxylic acids are compounds of biological importance and their decarboxylation is a significant biological process[1]. Chemically such decarboxylations at least for the more reactive acids such as mesoxalic, glyoxalic, oxaloacedic, pyruvic and dioxogulonic, are promoted by metal ions and/or primary amines[2]. In the chemical transamination process Schiff bases have been invoked as intermediates and the direction of decarboxylation is influenced by the nature of the substituents on the parent compounds[3]. In these nonenzymic decarboxylations usually aldehydes are formed as byproducts in variety of yields which under the reaction conditions resulted in condensation products.

Herein we wish to report a new and facile conversion of α-oxocarboxylic acids which carry enolizable hydrogens to enamines of aldehydes and subsequently to aldehydes or their derivatives in high yields.

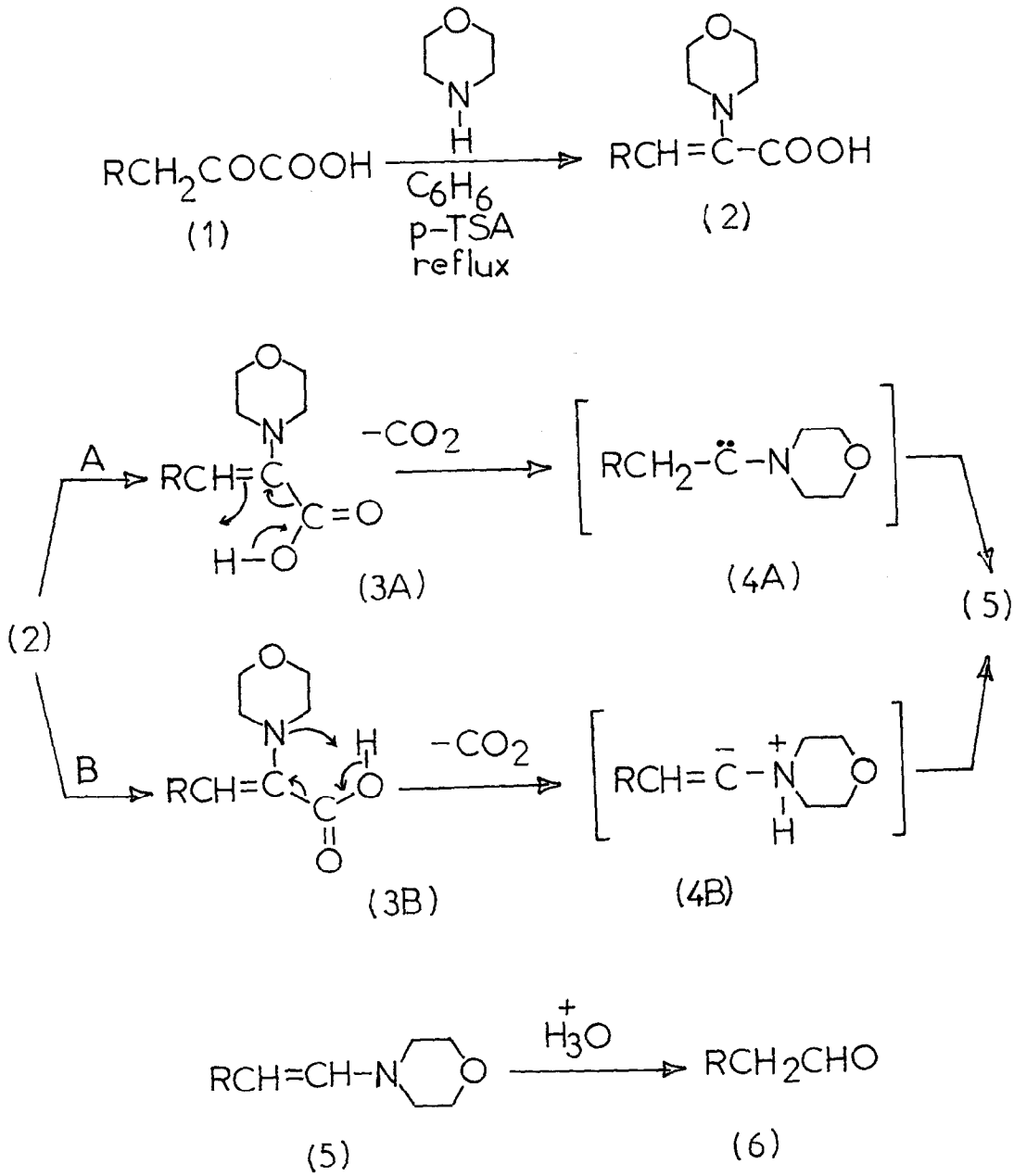
Aldehyde-enamines, which as a rule are prepared from the corresponding aldehydes, are versatile organic intermediates[4]. The enamine versatility in combination with the recent developments in the preparation of α-oxocarboxylic acids[5] could be of potential synthetic value in the construction of complex or delicate molecules such as the α,β-unsaturated aldehydes[4c].

The decarboxylation proceeds smoothly even when an aryl pyruvic acid carries strong electron withdrawing groups on the aromatic ring such as entries 1b, 1e, 1g and 1h, in contrast to the glycidic acid analogs which would not decarboxylate even at elevated temperatures[6].

A possible pathway in the formation of enamines (5) is shown in the Scheme and involves intermediate dehydroaminoacid derivative (2) which would decarboxylate[7] through (3A) to carbene (4A) and/or (3B) to betaine (4B). Rearrangement of (4A) and/or (4B) would form the enamine (5)[8].

The reaction conditions are mild, the procedure simple, analogous to the conventional procedure of preparation of enamines[9], and the transformation quantitative. In a typical experiment, into a solution or suspension of the α-oxoacid[11] in benzene (usually for 0.1 mole of α-oxoacid is used 100-150 ml benzene) is added 1.1 molar equivalents of morpholine and catalytic amount of p-toluenesulfonic acid[12]. The reaction mixture is refluxed under stirring with removal of water

SCHEME


RCH2COCOOH
(1)
C6H6
p-TSA
reflux
RCH=C-COOH
(2)
A
B
-CO2
(3A)
(4A)
(3B)
(4B)
(5)
H3O+
RCH2CHO
(6)

azeotropically either in a Dean-Stark thimble or by simple distillation the excess benzene. The progress of the reaction is monitored by Infrared Spectroscopy. The clear enamine[13] solution can be used directly in the next step. For obtaining the aldehyde, acidified water is added and the two layers stirred vigorously at room temperature for about an hour. The organic layer is dried, filtered through silica and the solvent evaporated.

TABLE $RCH_2COCOOH \longrightarrow RCH_2CHO$

α-OXOCARBOXYLIC ACID			ALDEHYDE	
Entry	R	Ref.	Isolated yield (%)	
1a	Phenyl	10a	94	
1b	2-Nitrophenyl	10b	84	Oxime m.p. 106-7°C, lit. m.p. 110°C (14)
1c	2-Methoxyphenyl	10c	100	Oxime m.p. 87-90°C
1d	4-Methoxyphenyl	10d	100	
1e	4-Chlorophenyl	10e	95	
1f	3,4-Dimethoxyphenyl	10f	99	
1g	2-Nitro-3-methoxy-phenyl	10g	88	Oxime m.p. 104-6°C, 2,4-DNFH, m.p. 153-4°C
1h	2-Nitro-5-methoxy-phenyl	10g	93	
1f	$CH_3(CH_2)_{15}$	10h	100	
1j	$CH_3(CH_2)_5$	10h	100	

New compounds have been characterized by analytical and spectroscopic means. Known products have been identified by comparison of their physical and spectroscopic properties with those of literature.

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11. In some instances α-oxocarboxylic acids were obtained as mixture with their isomeric α-hydroxycinnamic acids and were used as such.
12. For entries 1b, 1e, 1g and 1h the decarboxylation is considerably faster using two molar equivalents of morpholine and increased amount of catalyst.
13. The enamines were characterized by I.R. and N.M.R. Spectroscopy.
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